Techniques in Microfluidics: Creation of Microspheres for Cellular Encapsulation

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BACKGROUND

With innovations in stem cell research, cell therapy as a treatment modality has broad potential. Current pursuits range from diabetes and cardiovascular disorders to wound healing and aesthetic medicine. For stem cell therapy to be realized, a reliable method for transplanting cells is critical. Currently, technical difficulties including mechanical shearing and failure of a cell to engraft, limit the long-term survival of transplanted cells. Microencapsulation of cells within a protective biosphere allows cells to be safely injected into the host where they can proliferate and engraft providing therapeutic benefit. Alginate has been widely used for encasement of cells due to its natural tendency to create a biogel in the presence of calcium chloride. This abstract describes a novel strategy by which microfluidic molds are use to create a two layered system. In this model a protective alginate coating encapsulates cells suspended within collagen matrix. The ability of cells to proliferate within this protected environment has implications for cell transplant therapy.

HYPOTHESIS

- Microfluidic molds can be used to create uniform microspheres from biologically inert substances
- Cells will proliferate within this three-dimensional culture system

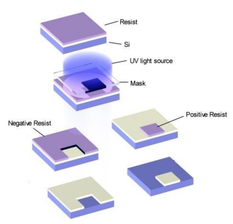
MATERIALS

- Polydimethylsiloxane (PDMS) *Sylgard® Dow Corninig Corporation Midland, MI*
- Type 1 bovine collagen *PureCol™ Inamed, Freemont, CA*
- Sodium Alginate
- Olive oil
- Mouse Hepatocyte Cell Line *AML12 ATCC Manassas, VA*

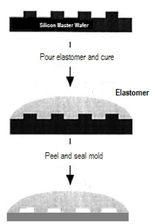
METHODS

PDMS Molds Created Using Lithography

1 Photolithography



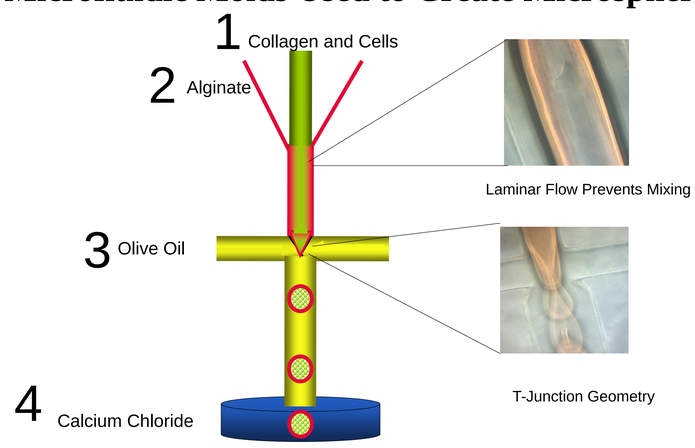
2 Softlithography



Ref: http://britneyspears.ac/physics/fabrication/image46.jpg

1. Patterned silicone templates created using photolithography
2. PDMS molds created from the silicone templates

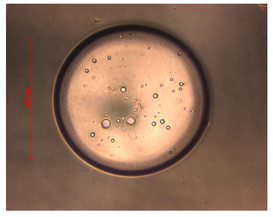
Microfluidic Molds Used to Create Microspheres



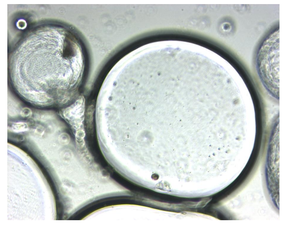
1. Cells are suspended in collagen and pumped through mold
2. Sodium alginate coats the collagen and cells. A low Reynolds number prevents mixing.
3. Using T-junction geometry, olive oil, an immiscible fluid, pinches the cylinder into spheres
4. Sodium Alginate crosslinks with Calcium Chloride as the microspheres enter collecting bath creating a protective shell
Collagen within the microspheres also gels within the heated (37°C) bath
5. Microspheres are incubated with nutrient rich media
6. Cell proliferation is documented using phase contrast imaging

RESULTS

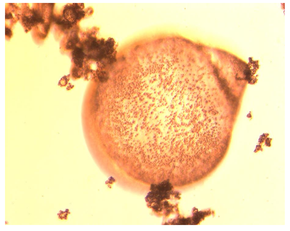
Cells Encapsulated Within Microspheres



Cells Proliferate Within Microspheres



Day 1



Day 15

CONCLUSIONS

- Microfluidic molds can be used to create uniform microspheres from biologically inert substances
- Cells can be encapsulated within these microspheres
- Hepatic cells survive and proliferate within this microenvironment for up to 2 weeks in culture